```
=> d his

     (FILE 'HOME' ENTERED AT 20:02:06 ON 19 MAR 2004)

     FILE 'REGISTRY' ENTERED AT 20:03:08 ON 19 MAR 2004
L1                STRUCTURE UPLOADED
L2              0 S L1 SSS SAM
L3             18 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 20:03:59 ON 19 MAR 2004
L4             34 S L3
L5              7 S L4 AND HYPERTENS?
L6              7 S L4 AND (HYPERTENS? OR HIGH(5A)BLOOD(5A)PRESSURE?)

     FILE 'STNGUIDE' ENTERED AT 20:06:50 ON 19 MAR 2004

     FILE 'STNGUIDE' ENTERED AT 20:11:56 ON 19 MAR 2004

     FILE 'REGISTRY' ENTERED AT 20:12:45 ON 19 MAR 2004
L7                STRUCTURE UPLOADED
L8              0 S L7 SSS SAM
L9              1 S L7 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 20:13:21 ON 19 MAR 2004
L10             1 S L9
L11             5 S L4 AND VASCULAR?

     FILE 'STNGUIDE' ENTERED AT 20:15:59 ON 19 MAR 2004

     FILE 'HCAPLUS' ENTERED AT 20:16:25 ON 19 MAR 2004
L12            27 S L4 NOT L5
L13            25 S L12 NOT L11

     FILE 'STNGUIDE' ENTERED AT 20:17:25 ON 19 MAR 2004
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Uploading C:\Program Files\Stnexp\Queries\hyper.str

L1       STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
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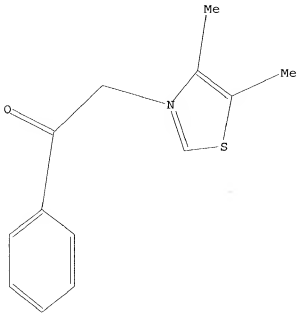

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Structure attributes must be viewed using STN Express query preparation.


=> s l1 sss sam
SAMPLE SEARCH INITIATED 20:03:29 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      8 TO ITERATE

100.0% PROCESSED       8 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             8 TO       329
PROJECTED ANSWERS:                0 TO         0

L2             0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 20:03:34 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    133 TO ITERATE

100.0% PROCESSED     133 ITERATIONS                               18 ANSWERS
SEARCH TIME: 00.00.01

L3            18 SEA SSS FUL L1
```

=> d l3 1

```
=> s l4 not l5
L12         27 L4 NOT L5

=> s l12 not l11
L13         25 L12 NOT L11

=> d l13 abs ibib hitrn 1-25
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L13 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Aging and diabetes mellitus (DM) both affect the structure and function of the myocardium, resulting in increased collagen in the heart and reduced cardiac function. As part of this process, hyperglycemia is a stimulus for the production of advanced glycation end products (AGEs), which covalently modify proteins and impair cell function. The goals of this study were first to examine the combined effects of aging and DM on hemodynamics and collagen types in the myocardium in 12 dogs, 9-12 yr old, and second to examine the effects of the AGE crosslink breaker phenyl-4,5-dimethylthazolium chloride (ALT-711) on myocardial collagen protein content, aortic stiffness, and left ventricular (LV) function in the aged diabetic heart. The alloxan model of DM was utilized to study the effects of DM on the aging heart. DM induced in the aging heart decreased LV systolic function (LV ejection fraction fell by 25%), increased aortic stiffness, and increased collagen type I and type III protein content. ALT-711 restored LV ejection fraction, reduced aortic stiffness and LV mass with no reduction in blood glucose level (199±17 mg/dL), and reversed the upregulation of collagen type I and type III. Myocardial LV collagen solubility (%) increased significantly after treatment with ALT-711. These data suggest that an AGE crosslink breaker may have a therapeutic role in aged patients with DM.

ACCESSION NUMBER: 2004:1425 HCAPLUS
DOCUMENT NUMBER: 140:91894
TITLE: Glycation end-product cross-link breaker reduces collagen and improves cardiac function in aging diabetic heart
AUTHOR(S): Liu, Jing; Masurekar, Malthi R.; Vatner, Dorothy E.; Jyothirmayi, Garikiparthy N.; Regan, Timothy J.; Vatner, Stephen F.; Meggs, Leonard G.; Malhotra, Ashwani
CORPORATE SOURCE: Department of Cell Biology and Molecular Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, NJ, 07101, USA
SOURCE: American Journal of Physiology (2003), 285(6, Pt. 2), H2587-H2591
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **341028-37-3**, ALT-711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycation end-product crosslink breaker reduces collagen and improves cardiac function in aging diabetic heart)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB The invention relates to the discovery that 3-deoxyglucosone (3DG) and other alpha-dicarbonyl sugars associated diseases and disorders are present and produced in the skin. Further, the invention relates to the discovery that amadorase, an enzyme that mediates 3DG synthesis, is also present in the skin. Thus, the invention further relates to methods of inhibiting production and function of 3-deoxyglucosone and other alphadicarbonyl sugars in skin thereby treating or prevention various diseases, disorders or conditions. Addnl., the invention relates to treatment of various diseases, disorders or conditions associated with or mediated by oxidative stress since 3DG induces ROS and AGEs, which are associated with the inflammatory response caused by oxidative stress.

ACCESSION NUMBER: 2003:856039 HCAPLUS
DOCUMENT NUMBER: 139:369668
TITLE: Inhibition of 3-deoxyglucosone and α-dicarbonyl sugars in skin and therapeutic uses for oxidative stress related diseases
INVENTOR(S): Tobia, Annette; Kappler, Francis
PATENT ASSIGNEE(S): Dynamis Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 192 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089601	A2	20031030	WO 2003-US12003	20030417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003219440	A1	20031127	US 2002-198706	20020718

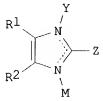
PRIORITY APPLN. INFO.: US 2002-373103P P 20020417
US 2002-392530P P 20020627
US 2002-198706 A 20020718

OTHER SOURCE(S): MARPAT 139:369668

IT **181069-80-7 181069-84-1**
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of 3-deoxyglucosone and α-dicarbonyl sugars in skin and therapeutic uses for oxidative stress related diseases)

L13 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

GI



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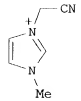


II

AB Title compds. I•X- [wherein M = cycloalkyl; X = pharmaceutically acceptable anion; Y = NH2 or CHR5R6; Z = H, alkyl, (hetero)arylmethyl, (un)substituted amino, etc.; R1 and R2 = independently H, acylamino, acyloxyalkyl, alkanoyl(alkyl), alkenyl, alkoxy, alkoxycarbonyl(alkyl), alkyl(amino), alkylenedioxy, ally, (dialkyl)amino, ω-alkylenesulfonic acid, carbamoyl, carboxy(alkyl), cycloalkyl, halo, hydroxy(alkyl), SH, NO2, alkylsulfinyl, alkylthio, CF3, azetidinyl, (thio)morpholinyl, (aryl)piperidinyl, arylpiperazinyl, or (hetero)aryl, etc.; or R1R2 = methylenedioxy or their ring carbons form a fused cycloalkyl, heteroaryl, or heterocycle; R5 = H, (cyclo)alkyl, alkenyl, alkynyl, (dialkyl)aminoalkyl, piperidinylalkyl, pyrrolidinylalkyl, azetidinylalkyl, alkylpiperazinylalkyl, etc.; R6 = H, (un)substituted alkyl, alkenyl, alkynyl, CN, (hetero)aryl, etc.; or pharmaceutically acceptable salts thereof] were prepared for breaking, reversing, or inhibiting the formation of advanced glycation endproducts (AGE) or AGE-mediated crosslinks (no data). For example, the exothermic reaction 1-methylimidazole with bromoacetonitrile produced II•Br-. Thus, I•X- and their pharmaceutical compns. are useful for treating or ameliorating fibrotic diseases or other indications in an animal, including a human (no data).

ACCESSION NUMBER: 2003:737371 HCAPLUS
DOCUMENT NUMBER: 139:261297
TITLE: Method for treating fibrotic diseases or other indications with imidazolium agents
INVENTOR(S): Wagle, Dilip; Vasan, Sara; Gall, Martin
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U. S. Ser. No. 38,112.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003176426	A1	20030918	US 2003-354952		20030130
US 2002068729	A1	20020606	US 2001-905188		20010713
US 2002160993	A1	20021031	US 2001-38112		20011231
US 2002177586	A1	20021128	US 2001-37447		20011231
PRIORITY APPLN. INFO.:			US 2000-218273P	P	20000713
			US 2000-259426P	P	20001229
			US 2000-259431P	P	20001229
			US 2001-259242P	P	20010102
			US 2001-296257P	P	20010606
			US 2001-296435P	P	20010606
			US 2001-905188	A2	20010713

US 2001-307418P P 20010724
US 2001-38112 A2 20011231
OTHER SOURCE(S): MARPAT 139:261297
IT **393121-34-1DP**, salts
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(AGE inhibitor; preparation of imidazolium AGE receptor inhibitors for treating fibrotic diseases or other indications)

L13 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB The formation of advanced glycation end products (AGEs) on extracellular matrix components leads to accelerated increases in collagen cross linking that contributes to myocardial stiffness in diabetes. This study determined the effect of the crosslink breaker, ALT-711 on diabetes-induced cardiac disease. Streptozotocin diabetes was induced in Sprague-Dawley rats for 32 wk. Treatment with ALT-711 (10 mg/kg) was initiated at week 16. Diabetic hearts were characterized by increased left ventricular (LV) mass and brain natriuretic peptide (BNP) expression, decreased LV collagen solubility, and increased collagen III gene and protein expression. Diabetic hearts had significant increases in AGEs and increased expression of the AGE receptors, RAGE and AGE-R3, in association with increases in gene and protein expression of connective tissue growth factor (CTGF). ALT-711 treatment restored LV collagen solubility and cardiac BNP in association with reduced cardiac AGE levels and abrogated the increase in RAGE, AGE-R3, CTGF, and collagen III expression. The present study suggests that AGEs play a central role in many of the alterations observed in the diabetic heart and that cleavage of preformed AGE crosslinks with ALT-711 leads to attenuation of diabetes-associated cardiac abnormalities in rats. This provides a potential new therapeutic approach for cardiovascular disease in human diabetes.
ACCESSION NUMBER: 2003:274376 HCAPLUS
DOCUMENT NUMBER: 139:207499
TITLE: A Breaker of Advanced Glycation End Products Attenuates Diabetes-Induced Myocardial Structural Changes
AUTHOR(S): Candido, Riccardo; Forbes, Josephine M.; Thomas, Merlin C.; Thallas, Vicki; Dean, Rachael G.; Burns, Wendy C.; Tikellis, Christos; Ritchie, Rebecca H.; Twigg, Stephen M.; Cooper, Mark E.; Burrell, Louise M.
CORPORATE SOURCE: Division of Diabetes, Lipoproteins, and Metabolism, Baker Heart Research Institute, Victoria, Australia
SOURCE: Circulation Research (2003), 92(7), 785-792
CODEN: CIRUAL; ISSN: 0009-7330
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **341028-37-3**, ALT 711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT-711 inhibition of AGE crosslinking attenuates diabetes-induced myocardial structural changes)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB A review. The role of advanced glycation end products (AGES) in diabetic

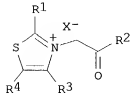
nephropathy has been developed during several years of research and increasingly complex AGE biochem. However, the structural diversity of AGE chemical has created new challenges in the search for AGE-based inhibition therapies. The challenges include the need to standardize measurements of serum and tissue AGE levels, identifying nephrotoxic AGE compds., understanding the cell biol. state of AGES in the diabetic kidney, determining the mechanism of action of selective inhibition of the glycation cascade, and forming complementary therapies. Current challenges in the development of new therapies for AGE nephrotoxicity are reviewed.

ACCESSION NUMBER: 2003:252556 HCAPLUS
DOCUMENT NUMBER: 139:332007
TITLE: New therapies for advanced glycation end product nephrotoxicity: current challenges
AUTHOR(S): Williams, Mark E.
CORPORATE SOURCE: Joslin Diabetes Center and Harvard Medical School, Boston, MA, USA
SOURCE: American Journal of Kidney Diseases (2003), 41(3, Suppl. 1), S42-S47
CODEN: AJKDDP; ISSN: 0272-6386
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
IT **181069-80-7**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; new therapies for advanced glycation end product nephrotoxicity)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB The purpose of this study was to investigate the effect of N-phenacyl-4,5-dimethylthiazolium bromide (DMPTB), an advanced glycation end product (AGE) cross-link breaker, on lens protein cross-links formed in vitro and in vivo. DMPTB was synthesized and its structure confirmed by its NMR spectrum. To show whether DMPTB can inhibit AGE crosslinking, recombinant human αA-crystallin was glycated with glucose-6-phosphate (G6P) in the presence and absence of DMPTB. Reversal of the already formed cross-links was studied by treating pre-glycated αA-crystallin with DMPTB. The ability of DMPTB to cleave in vivo formed cross-links was ascertained by treating water-insol. protein fractions from diabetic human lenses with this compound Glycation of αA-crystallin with G6P showed several high mol. weight (HMW) protein bands on the SDS-PAGE gel; DMPTB inhibited the formation of these HMW proteins. Mol. sieve HPLC confirmed the inhibition of formation of larger aggregates not separated by SDS-PAGE. Treatment of pre-glycated αA-crystallin with DMPTB gave evidence for the degradation of the already formed cross--linked HMW aggregates. Both mol. sieve HPLC and reverse-phase HPLC of the water-insol. protein fractions from two diabetic human lenses showed that DMPTB could degrade a major portion of the cross-linked HMW aggregates to lower mol. weight proteins. This suggests that the cross-linked proteins in human lenses are formed predominantly by the advanced glycation process and cross-link breakers like DMPTB may have application for the intervention of protein crosslinking in the eye lens.
ACCESSION NUMBER: 2002:958056 HCAPLUS
DOCUMENT NUMBER: 139:127787

TITLE: Cleavage of in vitro and in vivo formed lens protein cross-links by a novel cross-link breaker
AUTHOR(S): Hollenbach, Seth; Thampi, Prajitha; Viswanathan, Tito; Abraham, Edathara C.
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR, 72205, USA
SOURCE: Molecular and Cellular Biochemistry (2003), 243(1&2), 73-80
CODEN: MCBIB8; ISSN: 0300-8177
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **181069-80-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cleavage of lens protein cross-links by a novel cross-link breaker, N-phenacyl-4,5-dimethylthiazolium bromide, in vitro and in aged, diabetic human lenses)
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB A composition for the treatment of hair, nail, ex-vivo organ, ex-vivo cell or ex-vivo tissue to improve the biomech. and diffusional characteristics comprising an effective amount of title compds., e.g. [I; R1 = alkyl, CHR5OH, CHR5O2CR6; R5 = alkyl; R6 = alkyl, Ph, halophenyl, alkoxyphenyl, naphthyl; R2 = OH, Ph, halophenyl, alkoxyphenyl, (aromatic) heterocyclyl; R3, R4 = H, alkyl, hydroxyalkyl, Ph; R3R4 = atoms to form an (aromatic) (substituted) ring; X = halide, other pharmaceutically acceptable anion]. Thus, 2-aminopyrimidine in CH2Cl2 was treated dropwise with O-mesitylenesulfonylhydroxylamine in CH2Cl2 at 4° followed by stirring overnight to give 2,3-diaminopyrimidinium mesitylene-2-sulfonate salt. The latter at 10 nM gave 52% reversal of sugar-mediated coupling of albumen to collagen after 2 days.
ACCESSION NUMBER: 2002:615361 HCAPLUS
DOCUMENT NUMBER: 137:169535
TITLE: Preparation of azoles, azines and salts thereof for rejuvenating cells, tissues, organs, hair and nails.
INVENTOR(S): Ulrich, Peter C.; Fang, Sheng Ding; Brines, Michael; Xie, Qiao Wen; Cerami, Anthony

PATENT ASSIGNEE(S): Farrington Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062301	A2	20020815	WO 2002-US3714	20020207
WO 2002062301	A3	20021017		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002188015	A1	20021212	US 2002-72712	20020207
EP 1368029	A2	20031210	EP 2002-709416	20020207

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-267226P P 20010207
WO 2002-US3714 W 20020207

OTHER SOURCE(S): MARPAT 137:169535

IT **446839-56-1P**
RL: COS (Cosmetic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of azoles, azines and salts thereof for rejuvenating cells, tissues, organs, hair and nails)

IT **341028-37-3**
RL: COS (Cosmetic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of azoles, azines and salts thereof for rejuvenating cells, tissues, organs, hair and nails)

L13 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

ACCESSION NUMBER: 2002:556104 HCAPLUS
DOCUMENT NUMBER: 137:109489
TITLE: Compositions comprising a polypeptide and an active agent
INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002099013	A1	20020725	US 2001-933708	20010822
PRIORITY APPLN. INFO.:			US 2000-247556P P	20001114
			US 2000-247558P P	20001114
			US 2000-247559P P	20001114
			US 2000-247560P P	20001114
			US 2000-247561P P	20001114
			US 2000-247594P P	20001114
			US 2000-247595P P	20001114
			US 2000-247606P P	20001114
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			US 2000-247608P P	20001114
			US 2000-247609P P	20001114
			US 2000-247610P P	20001114
			US 2000-247611P P	20001114
			US 2000-247612P P	20001114
			US 2000-247620P P	20001114
			US 2000-247621P P	20001114
			US 2000-247634P P	20001114
			US 2000-247635P P	20001114
			US 2000-247698P P	20001114
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			US 2000-247929P P	20001114
			US 2000-247930P P	20001114

IT **181069-80-7**, ALT 711
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

L13 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB A composition for the treatment of hair, nail, ex-vivo organ, ex-vivo cell or ex-vivo tissue to improve the biomech. and diffusional characteristics comprises a thiazolium compound Thus, a shampoo contained 30% sodium lauryl

sulfate 40.00, lauric diethanolamide 4.00, 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium chloride 1.10, perfume 0.25, Dowicil-200 0.20 and soft water 54.45% by weight

ACCESSION NUMBER: 2002:555309 HCAPLUS
DOCUMENT NUMBER: 137:114210
TITLE: Compositions containing thiazolium compound for rejuvenating hair, nails, tissues, cells and organs
INVENTOR(S): Brines, Michael L.; Cerami, Anthony
PATENT ASSIGNEE(S): Farrington Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002056836	A2	20020725	WO 2002-US1860	20020122
WO 2002056836	A3	20021212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002182165	A1	20021205	US 2002-55252	20020122
US 2003185776	A1	20031002	US 2003-392450	20030318

PRIORITY APPLN. INFO.: US 2001-263300P P 20010122
US 2002-55252 A1 20020122

OTHER SOURCE(S): MARPAT 137:114210

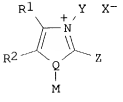
IT **341028-37-3 393121-34-1**
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing thiazolium compound for rejuvenating hair and nails and tissues and cells and organs)

L13 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB A review. Recent studies have revealed that reducing sugars, such as glucose, react with proteins through non-enzymic glycosylation to form irreversible, covalently crosslinked proteins known as advanced glycation endproducts (AGEs). Furthermore, it has been demonstrated that this naturally occurring process, accelerated in diabetics due to hyperglycemia, impairs biol. functions leading to cardiovascular disorders, as well as diabetic and age-related complications. Pharmaceutical intervention to prevent or reverse these complications have focused on inhibiting the formation of AGEs by compds. such as dimethyl-3-phenacylthiazolium chloride or breaking the glucose derived crosslinks by selective cleavage. Intervention targeted at AGE crosslinks in vivo offers a way to interfere with age-related changes of tissues.

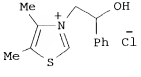
ACCESSION NUMBER: 2002:527729 HCAPLUS
DOCUMENT NUMBER: 138:100199
TITLE: Pharmaceutical intervention of advanced glycation

endproducts
AUTHOR(S): Cerami, Anthony; Ulrich, Peter
CORPORATE SOURCE: The Kenneth S. Warren Laboratories, Tarrytown, NY, 10591, USA
SOURCE: Novartis Foundation Symposium (2001), 235(Aging Vulnerability), 202-216
CODEN: NFSYF7; ISSN: 1528-2511
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
IT **341028-37-3**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemical of advanced glycation endproducts formation, role of advanced glycation endproducts in age-related complications and pharmacol. intervention)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II

AB Provided is a method of decreasing intraocular pressure or improving ocular accommodation comprising administering I [R1-2 = H, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, etc.; Z = H, alkyl, Ar-CH2, NR3R4, etc.; R3-4 = H, alkyl, Ar, Ar-alkyl; Ar = (hetero)aryl; Y = amino, CHR5R6; R5 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aminoalkyl, etc.; R6 = H, alk(en/yn)yl, cyano, aryl/heterocycle, etc.; Q = N, O, S; M is absent when Q = O, S; M = alkyl, vinyl, allyl, Y; X = pharmaceutically acceptable anion]. Examples include, 11 compds., effect of example compds. on outflow facility primates, drug penetration studies on intact cornea (rabbit, monkey), effect of compds. on i.m. pilocarpine-stimulated accommodative response (monkey) and the ability of test compds. to inhibit crosslinking (and reverse already formed cross linking) of glycated serum albumin to rat tail tendon collagen (which prevent outflow). For instance, 2-Chloro-1-phenylethanol (preparation given) was used to alkylate 4,5-dimethylthiazole (neat, 135°, 28 h) to afford II (9.7%) as prisms, mp 201-203°. I are useful in the treatment/prevention of glaucoma.
ACCESSION NUMBER: 2002:521491 HCAPLUS
DOCUMENT NUMBER: 137:78956
TITLE: Synthesis of thiazolium and imidazolium salts and use in treating glaucoma
INVENTOR(S): Egan, John J.; Wagle, Dilip; Vasan, Sara; Gall,

Martin; Bell, Stanley C.; Lavoie, Edmond J.
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053158	A1	20020711	WO 2001-US49550	20011228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1353669	A1	20031022	EP 2001-988353	20011228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-259426P P 20001229
US 2001-296257P P 20010606
US 2001-307418P P 20010724
WO 2001-US49550 W 20011228

OTHER SOURCE(S): MARPAT 137:78956
IT **356759-45-0P 356759-46-1P 356759-47-2P**
356759-50-7P 356759-52-9P 356759-53-0P
393121-65-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiglaucoma agent; synthesis of thiazolium and imidazolium salts as antiglaucoma agents)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB Background: Crosslinking of macromols. like collagen plays an important role in the development of complications in diabetes and ageing. One of the underlying mechanisms of this crosslinking is the formation of advanced glycation endproducts (AGEs). Methods: In this study, we assessed the use of differential scanning calorimetry (DSC) for the determination of these cross-links and the effects of an AGE inhibitor and breaker. Results: Treatment with N-phenacylthiazolium bromide (ALT-711) of diabetic rats with 2 mo duration of diabetes normalized large artery stiffness, assessed by characteristic input impedance and systemic arterial compliance, but with the use of DSC, no statistical difference in crosslinking between control and treated animals could be measured. In addition, we performed in vitro incubation of collagen prepns. with ribose and glucose to assess the DSC method as well as the influence of AGE breakers and inhibitors. Incubation of rat tail tendon (RTT) with 100 mmol/l glucose showed an increase in collagen crosslinking expressed as an

increase in shrinkage temperature (Ts). Addition of aminoguanidine (AG), an inhibitor of AGE formation, prior to glucose incubation showed a slower increase of the amount of glucose-derived crosslinking. Replacing glucose with ribose showed a quicker increase in crosslinking and less effect on crosslinking by adding aminoguanidine, demonstrating the higher reactivity of pentoses above hexoses. Similar expts. with rat skin samples (RSS) showed that RSS (type III collagen) are less susceptible to glucose-mediated crosslinking than RTT (type I collagen). We observed no effect of addition of ALT-711, a breaker of glucose-derived cross-links, on the extent of collagen crosslinking in both RTT and RSS. Conclusion: Overall, DSC is considered a useful method for assessing glucose-mediated crosslinking in vitro with nonphysiol. glucose concns. The in vivo use in biol. samples is limited due to the lack of sensitivity. However, DSC remains a quick and well-quantitated method in comparison with other methods, like enzymic digestibility.

ACCESSION NUMBER: 2002:380419 HCAPLUS
DOCUMENT NUMBER: 137:137181
TITLE: Glucose-mediated cross-linking of collagen in rat tendon and skin
AUTHOR(S): Mentink, Cyriel J. A. L.; Hendriks, Marc; Levels, Anita A. G.; Wolffenbuttel, Bruce H. R.
CORPORATE SOURCE: Department of Endocrinology, Maastricht University Hospital, Maastricht, 6202 AZ, Neth.
SOURCE: Clinica Chimica Acta (2002), 321(1-2), 69-76
CODEN: CCATAR; ISSN: 0009-8981
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **181069-80-7**, ALT-711
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glucose-mediated crosslinking of collagen in rat tendon and skin)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

ACCESSION NUMBER: 2002:332011 HCAPLUS
DOCUMENT NUMBER: 136:355482
TITLE: Compositions comprising a polypeptide and an active agent
INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J.
PATENT ASSIGNEE(S): New River Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002034237	A1	20020502	WO 2001-US26142	20010822	

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001086599	A5	20020506	AU 2001-86599	20010822	
EP 1311242	A1	20030521	EP 2001-966056	20010822	

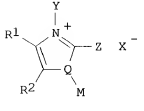
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:		US 2000-642820	A 20000822
		WO 2001-US26142	W 20010822

IT **181069-80-7**, ALT 711
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB Provided among other things is a method of treating or ameliorating or preventing an indication of the invention in an animal, including a human, comprising administering an effective amount of I. Rats treated with 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt had smaller weight of infarcted heart tissue with reduced thickness of ventricular wall in infarcted zone.

ACCESSION NUMBER:	2002:89829 HCAPLUS
DOCUMENT NUMBER:	136:129060
TITLE:	Method for treating fibrotic diseases or other indications IC
INVENTOR(S):	Egan, Jack; Wagle, Dilip; Vasan, Sarah; Gall, Martin
PATENT ASSIGNEE(S):	Alteon, Inc., USA
SOURCE:	PCT Int. Appl., 72 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002007725	A1	20020131	WO 2001-US22214	20010713	
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,				
	RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,				
	VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				
	BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002103182	A1	20020801	US 2001-905035	20010713	
US 6610716	B2	20030826			
EP 1305024	A1	20030502	EP 2001-958946	20010713	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004504348	T2	20040212	JP 2002-513460	20010713	
PRIORITY APPLN. INFO.:			US 2000-218273P	P	20000713
			US 2000-259431P	P	20001229
			US 2001-259242P	P	20010102
			US 2001-296435P	P	20010606
			WO 2001-US22214	W	20010713

OTHER SOURCE(S): MARPAT 136:129060

IT **393121-34-1D**, salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating fibrotic diseases or other indications)

IT **356759-45-0P 356759-46-1P 356759-47-2P**
356759-50-7P 356759-52-9P 356759-53-0P
393121-65-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(treating fibrotic diseases or other indications)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB The advanced glycation end-product (AGE) hypothesis proposes that accelerated chemical modification of proteins by glucose during hyperglycemia contributes to the pathogenesis of diabetic complications. The two most commonly measured AGEs, Nε-(carboxymethyl)lysine and pentosidine, are glycoxidn. products, formed from glucose by sequential glycation and autoxidn. reactions. Although several compds. have been developed as AGE inhibitors and are being tested in animal models of diabetes and in clin. trials, the mechanism of action of these inhibitors is poorly understood. In general, they are thought to function as nucleophilic traps for reactive carbonyl intermediates in the formation of AGEs; however alternative mechanisms of actions, such as chelation, have not been rigorously examined To distinguish between the carbonyl trapping and antioxidant activity of AGE inhibitors, we have measured the chelating activity of the inhibitors by determining the concentration required for 50% inhibition of the rate of copper-catalyzed autoxidn. of ascorbic acid in phosphate buffer. All AGE inhibitors studied were chelators of copper, as measured by inhibition of metal-catalyzed autoxidn. of ascorbate. Apparent binding consts. for copper ranged from ~2 mM for aminoguanidine and pyridoxamine, to 10-100 μM for carnosine, phenazinediamine, OPB-9195 and tenilsetam.

The AGE-breakers, phenacylthiazolium and phenacyldimethylthiazolium bromide, and their hydrolysis products, were among the most potent inhibitors of ascorbate oxidation We conclude that, at millimolar concns. of AGE inhibitors used in many in vitro studies, inhibition of AGE formation results primarily from the chelating or antioxidant activity of the AGE inhibitors, rather than their carbonyl trapping activity. Further, at therapeutic concns., the chelating activity of AGE inhibitors and AGE-breakers may contribute to their inhibition of AGE formation and protection against development of diabetic complications.

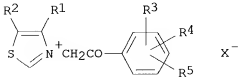
ACCESSION NUMBER: 2002:43332 HCAPLUS
DOCUMENT NUMBER: 136:288862
TITLE: Chelating activity of advanced glycation end-product inhibitors
AUTHOR(S): Price, David L.; Rhett, Patricia M.; Thorpe, Suzanne R.; Baynes, John W.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of South Carolina, Columbia, SC, 29208, USA
SOURCE: Journal of Biological Chemistry (2001), 276(52), 48967-48972
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **181069-80-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chelating activity of advanced glycation end-product inhibitors)
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB A review. Glucose and other reducing sugars react non-enzymically with proteins leading to the formation of advanced glycosylation end products (AGEs) and AGE-derived protein crosslinking. Formation of AGEs is a normal physiol. process, which is accelerated under the hyperglycemic condition in diabetes. Under normal conditions, AGEs build up slowly and accumulate as one ages. Numerous studies have indicated that AGEs contribute to the pathol. events leading to diabetic complications, such as age-related diseases, including nephropathy, retinopathy, vasculopathy and neuropathy. Potential therapeutic approaches to prevent these complications include pharmacol. inhibition of AGE formation and disruption of pre-formed AGE-protein cross-links. Studies using animal models and preliminary clin. trials have shown the ability of the AGE-inhibitor, pimagedine and the cross-link breaker, ALT-711, to reduce the severity of pathologies of advanced glycosylation. These agents offer potential treatments for glucose-derived complications of diabetes and ageing.

ACCESSION NUMBER: 2001:849132 HCAPLUS
DOCUMENT NUMBER: 136:128484
TITLE: Therapeutic potential of AGE inhibitors and breakers of AGE protein cross-links
AUTHOR(S): Vasan, Sara; Foiles, Peter G.; Founds, Henry W.
CORPORATE SOURCE: Alteon, Inc., Ramsey, NJ, 07446, USA
SOURCE: Expert Opinion on Investigational Drugs (2001), 10(11), 1977-1987
CODEN: EOIDER; ISSN: 1354-3784

PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
1T **341028-37-3**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic potential of AGE inhibitors and breakers of AGE protein cross-links)
REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB Title compds. I (R1, R2 = H, alkyl, hydroxyalkyl; R3, R4, R5 = H, alkyl, alkoxy, halo; X is a leaving group) were prepared by reaction of thiazoles with R3R4R5C6H2COCH2X in solvents having a dielec. constant at 20° of 30-40. Thus, 9.52 kg of 4,5-dimethylthiazole and 13.00 kg of 2-chloroacetophenone were refluxed in MeCN under N for 96.5 h to give 17.99 kg of 4,5-dimethyl-3-(2-oxo-2-phenylethyl)thiazolium chloride, which was subjected to a purification process.
ACCESSION NUMBER: 2001:730717 HCAPLUS
DOCUMENT NUMBER: 135:272952
TITLE: Synthesis of thiazolium compounds
INVENTOR(S): Wagle, Dilip
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072724	A1	20011004	WO 2001-US10355	20010329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002013471	A1	20020131	US 2001-821846	20010329
US 6506902	B2	20030114		

PRIORITY APPLN. INFO.: US 2000-192867P P 20000329
OTHER SOURCE(S): CASREACT 135:272952; MARPAT 135:272952
IT **341028-37-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB Prolonged hyperglycemia inhibits B-cell function by mechanisms that are largely unclarified. We investigated the involvement of advanced glycation end products (AGEs), using aminoguanidine as well as the AGE-breaking compound ALT-711 in a transplantation model. Islets from Wistar-Furth rats were transplanted under the kidney capsule of syngeneic streptozocin-diabetic recipients. Aminoguanidine was administered as 1 g/L in the drinking water. Graft-bearing kidneys were isolated and perfused to investigate insulin secretion, and grafts were excised to measure preproinsulin mRNA contents. In all transplants to diabetic rats, insulin responses to 27.8 mM glucose were abolished and aminoguanidine failed to correct this abnormality. However, aminoguanidine treatment for 8 wk following transplantation increased preproinsulin mRNA contents of the grafts ($P < 0.05$). In addition, treatment with aminoguanidine enhanced the insulin secretory response to arginine ($P < 0.05$). Arginine-induced insulin secretion was also enhanced when aminoguanidine treatment was started after an initial 2-wk implantation period rather than immediately after transplantation. On the other hand, treatment with ALT-711 (0.1 mg/kg by gavage) for 8 wk completely failed to affect B-cell function of grafts, and ALT-711 was also ineffective under in vitro conditions. Our findings indicate that aminoguanidine effects in vivo are to a major extent not coupled to AGEs or nitric oxide synthetase inhibition, but possibly to oxidative modifications accomplished by the guanidine compound
ACCESSION NUMBER: 2000:345369 HCAPLUS
DOCUMENT NUMBER: 133:114896
TITLE: Improvement by aminoguanidine of insulin secretion from pancreatic islets grafted to syngeneic diabetic rats
AUTHOR(S): Hiramatsu, S.; Inoue, K.; Tajirl, Y.; Grill, V.
CORPORATE SOURCE: Endocrine and Diabetes Unit, Department of Molecular Medicine, Karolinska Hospital, Karolinska Institute, Stockholm, S-17176, Swed.
SOURCE: Biochemical Pharmacology (2000), 60(2), 263-268
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **181069-80-7**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(improvement by aminoguanidine of insulin secretion from pancreatic islets grafted to syngeneic diabetic rats)
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB On page 2809, paragraph 1, line 23, the name of the cross-link breaker should be 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-thiazolium chloride instead of phenyl-4,5-dimethylthazolium chloride.

ACCESSION NUMBER: 2000:341544 HCAPLUS
DOCUMENT NUMBER: 134:51229
TITLE: An advanced glycation end-product cross-link breaker can reverse age-related increases in myocardial stiffness. [Erratum to document cited in CA132:329694]
AUTHOR(S): Asif, Mohammad; Egan, John; Vasan, Sara; Jyothirmayi, Garikiparthy N.; Masurekar, Malthi R.; Lopez, Santos; Williams, Chandra; Torres, Ramon L.; Wagle, Dilip; Ulrich, Peter; Cerami, Anthony; Brines, Michael; Regan, Timothy J.
CORPORATE SOURCE: New Jersey Medical School, Univ. Medicine and Dentistry New Jersey, Newark, NJ, 07103, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(10), 5679
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **181069-80-7**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(an advanced glycation endproduct cross-link breaker can reverse age-related increases in myocardial stiffness (Erratum))

L13 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB Decreased elasticity of the cardiovascular system is one of the hallmarks of the normal aging process of mammals. A potential explanation for this decreased elasticity is that glucose can react nonenzymically with long-lived proteins, such as collagen and lens crystallin, and link them together, producing advanced glycation endproducts (AGEs). Previous studies have shown that aminoguanidine, an AGE inhibitor, can prevent glucose crosslinking of proteins and the loss of elasticity associated with aging and diabetes. Recently, an AGE cross-link breaker (ALT-711) has been described, which we have evaluated in aged dogs. After 1 mo of administration of ALT-711, a significant reduction (≈40%) in age-related left ventricular stiffness was observed [(57.1 ± 6.8 mmHg·m2/mL pretreatment and 33.1 ± 4.6 mmHg·m2/mL posttreatment (1 mmHg = 133 Pa))]. This decrease was accompanied by improvement in cardiac function.
ACCESSION NUMBER: 2000:202230 HCAPLUS
DOCUMENT NUMBER: 132:329694
TITLE: An advanced glycation endproduct cross-link breaker can reverse age-related increases in myocardial stiffness
AUTHOR(S): Asif, Mohammad; Egan, John; Vasan, Sara; Jyothirmayi, Garikiparthy N.; Masurekar, Malthi R.; Lopez, Santos; Williams, Chandra; Torres, Ramon L.; Wagle, Dilip; Ulrich, Peter; Cerami, Anthony; Brines, Michael; Regan, Timothy J.
CORPORATE SOURCE: University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, NJ, 07103, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(6), 2809-2813
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal

LANGUAGE: English
IT **181069-80-7**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(an advanced glycation endproduct cross-link breaker can reverse age-related increases in myocardial stiffness)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
AB The present invention relates to compns. and methods for inhibiting and reversing nonenzymic crosslinking (protein aging). Accordingly, compns. are disclosed which comprise an agent capable of inhibiting the formation of advanced glycosylation endproducts of target proteins, and which addnl. reverse pre-formed crosslinks in the advanced glycosylation endproducts by cleaving alpha-dicarbonyl-based protein crosslinks present in the advanced glycosylation endproducts. Certain agents useful are thiazolium salts. The method comprises contacting the target protein with the composition Both industrial and therapeutic applications for the invention are envisioned, as food spoilage and animal protein aging can be treated. A novel immunoassay for detection of the reversal of the nonenzymic crosslinking is also disclosed.
ACCESSION NUMBER: 1999:25966 HCAPLUS
DOCUMENT NUMBER: 130:100661
TITLE: Thiazolium compounds for preventing and reversing the formation of advanced glycosylation endproducts
INVENTOR(S): Cerami, Anthony; Ulrich, Peter C.; Wagle, Dilip R.; Hwang, San-Bao; Vasan, Sara; Egan, John J.
PATENT ASSIGNEE(S): The Picower Institute for Medical Research, USA; Alteon Inc.
SOURCE: U.S., 30 pp., Cont.-in-part of U.S. Ser. No. 473,104, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5853703	A	19981229	US 1996-588249	19960118
US 5656261	A	19970812	US 1995-375155	19950118
CA 2210684	AA	19960725	CA 1996-2210684	19960118
WO 9622095	A2	19960725	WO 1996-US663	19960118
WO 9622095	A3	19970227		
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AZ, BY, KG, KZ, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9647599	A1	19960807	AU 1996-47599	19960118
AU 714607	B2	20000106		
EP 808163	A2	19971126	EP 1996-903540	19960118
EP 808163	B1	20030723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				

CN 1185736	A	19980624	CN 1996-192393	19960118	
JP 10512864	T2	19981208	JP 1996-522379	19960118	
BR 9607598	A	19991130	BR 1996-7598	19960118	
EP 1327887	A2	20030716	EP 2003-75955	19960118	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
AT 245420	E	20030815	AT 1996-903540	19960118	
PT 808163	T	20031231	PT 1996-96903540	19960118	
FI 9703031	A	19970915	FI 1997-3031	19970717	
NO 9703308	A	19970918	NO 1997-3308	19970717	
US 6007865	A	19991228	US 1997-971878	19971119	
US 38330	E	20031125	US 1999-373345	19990812	
US 6440749	B1	20020827	US 1999-470482	19991222	
US 2002192842	A1	20021219	US 2002-174883	20020619	
US 2004034074	A1	20040219	US 2003-418398	20030418	

PRIORITY APPLN. INFO.:

US 1995-375155	A2	19950118
US 1995-473104	B2	19950607
US 1995-473184	A	19950607
EP 1996-903540	A3	19960118
US 1996-588249	A	19960118
WO 1996-US663	W	19960118
US 1997-971878	A3	19971119
US 1999-470482	A3	19991222
US 2002-174883	A1	20020619

OTHER SOURCE(S): MARPAT 130:100661

IT **181069-80-7P 181069-84-1P 181070-56-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiazolium compds. for preventing and reversing the formation of advanced glycosylation endproducts)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Glucose and other reducing sugars react with proteins by a nonenzymic, posttranslational modification process called nonenzymic glycation. The formation of advanced glycation end products (AGEs) on connective tissue and matrix components accounts largely for the increase in collagen crosslinking that accompanies normal aging and which occurs at an accelerated rate in diabetes, leading to an increase in arterial stiffness. A new class of AGE crosslink "breakers" reacts with and cleaves these covalent, AGE-derived protein crosslinks. Treatment of rats with streptozotocin-induced diabetes with the AGE-breaker ALT-711 for 1-3 wk reversed the diabetes-induced increase of large artery stiffness as measured by systemic arterial compliance, aortic impedance, and carotid artery compliance and distensibility. These findings will have considerable implications for the treatment of patients with diabetes-related complications and aging.

ACCESSION NUMBER: 1998:267333 HCAPLUS

DOCUMENT NUMBER: 129:23234

TITLE: Breakers of advanced glycation end products restore large artery properties in experimental diabetes

AUTHOR(S): Wolffenbuttel, Bruce H. R.; Boulanger, Chantal M.; Crijns, Francy R. L.; Huijberts, Maya S. P.; Poitevin, Pierre; Swennen, Geertje N. M.; Vasan, Sara; Egan, John J.; Ulrich, Peter; Cerami, Anthony; Levy, Bernard

I.

CORPORATE SOURCE: Department of Endocrinology, Cardiovascular Research Institute Maastricht and University (Hospital) Maastricht, Maastricht, 6202 AZ, Neth.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(8), 4630-4634
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **181069-80-7**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(breakers of advanced glycation end products restore large artery properties in exptl. diabetes)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB The acid generators are obtained from specified aromatic onium borate compds. having substituted quaternary N-containing heterocyclic 5-membered ring cation moieties (which may have a second N, O or S atom at position distant from the 1st N atom such as imidazolium, oxazolium and thiazolium) and fluoro borate anion moieties bearing Ph groups substituted with electron-withdrawing groups, e.g., F, NO2, CN and azide groups, in place of previously known hexafluorophosphate and hexafluoroantimonate anions. The generators are used in compns. containing acid-curable compds., and optionally radical-polymerizable monomers, photosensitizers and radical initiators for speeding up their curing under radiation with energy beams. An example of the acid generator was N-benzylthiazolium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate; the mixture of 1 part of which with 100 parts 3,4-epoxycyclohexylmethyl 3,4-epoxycyclohexanecarboxylate (ERL-4221) could be cured with UV light.

ACCESSION NUMBER: 1997:617534 HCAPLUS
DOCUMENT NUMBER: 127:308066
TITLE: Odorless nontoxic energy beam-sensitive acid generators with good solubility, curable compositions containing them and cured products
INVENTOR(S): Toba, Yasumasa; Tanaka, Yasuhiro
PATENT ASSIGNEE(S): Toyo Ink Mfg. Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 39 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09241614	A2	19970916	JP 1996-45704	19960304

PRIORITY APPLN. INFO.: JP 1996-45704 19960304
OTHER SOURCE(S): MARPAT 127:308066

IT **197175-62-5P**, 2,4,5-Trimethyl-3-phenacylthiazolium tetrakis(pentafluorophenyl)borate
RL: CAT (Catalyst use); IMF (Industrial manufacture); PREP (Preparation); USES (Uses)

(odorless nontoxic energy beam-sensitive acid generators with good solubility, curable compns. containing them and cured products)

L13 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Compns. and methods for inhibiting and reversing nonenzymic crosslinking (protein aging) are disclosed. Accordingly, compositions are disclosed which comprise an agent capable of inhibiting the formation of advanced glycosylation endproducts of target proteins (such as thiazolium salts), and which addnl. reverse pre-formed crosslinks in the advanced glycosylation endproducts by cleaving α-dicarbonyl-based protein crosslinks present in the advanced glycosylation endproducts. Both industrial and therapeutic applications for the invention are envisioned, as food spoilage and animal protein aging can be treated. A novel immunoassay for detection of the reversal of the nonenzymic crosslinking is also disclosed. Thiazole 850 mg, Me bromoacetate 1.52 mg, and absolute ethanol 50 mL were refluxed for 2 h, then cooled and the salt separated and recrystd. to obtain 3-(2-methoxy-2-oxoethyl)-thiazolium bromide (I). A lotion contained I 1.0, ethanol 200.0, PEG-400 300.0, hydroxypropyl cellulose 5.0 mg, and propylene glycol q.s. 1.0 g.

ACCESSION NUMBER: 1996:560531 HCAPLUS
DOCUMENT NUMBER: 125:204548
TITLE: Use of thiazolium compounds for preventing and reversing the formation of advanced glycosylation endproducts
INVENTOR(S): Cerami, Anthony; Ulrich, Peter C.; Wagle, Dilip R.; Hwang, San-bao; Vasan, Sara; Egan, John J.
PATENT ASSIGNEE(S): Alteon Inc., USA; The Picower Institute for Medical Research
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622095	A2	19960725	WO 1996-US663	19960118
WO 9622095	A3	19970227		
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AZ, BY, KG, KZ, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5656261	A	19970812	US 1995-375155	19950118
AU 9647599	A1	19960807	AU 1996-47599	19960118
AU 714607	B2	20000106		
EP 808163	A2	19971126	EP 1996-903540	19960118
EP 808163	B1	20030723		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10512864	T2	19981208	JP 1996-522379	19960118
US 5853703	A	19981229	US 1996-588249	19960118
BR 9607598	A	19991130	BR 1996-7598	19960118
AT 245420	E	20030815	AT 1996-903540	19960118
FI 9703031	A	19970915	FI 1997-3031	19970717
NO 9703308	A	19970918	NO 1997-3308	19970717

US 38330	E	20031125	US 1999-373345		19990812
PRIORITY APPLN. INFO.:			US 1995-375155	A	19950118
			US 1996-588249	A	19960118
			US 1995-473104	B2	19950607
			US 1995-473184	A	19950607
			WO 1996-US663	W	19960118

OTHER SOURCE(S): MARPAT 125:204548

IT **181069-80-7P 181069-84-1P 181070-56-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of thiazolium compds. for preventing and reversing the formation of advanced glycosylation endproducts)

L13 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
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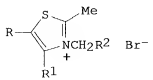

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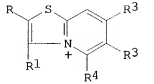

II

AB Condensation of 2-methylthiazolium salts I (R = H, Me; R1 = Me, Ph; RR1 = CH:CHCH:CH; R2 = Bz, CO2Et) with R3COCOR3 (R3 = e.g. Me, Ph) in the presence of base, yielded thiazolo[3,2-a]pyridinium derivs. II (R4 = H, R2). Results with different substrates are discussed.

ACCESSION NUMBER:	1987:515522 HCAPLUS
DOCUMENT NUMBER:	107:115522
TITLE:	2-Methylthiazolium salts as 1,4-dinucleophiles. Thiazolo[3,2-a]pyridinium salts from Westphal condensation
AUTHOR(S):	Galera, C.; Vaquero, J. J.; Garcia Navio, J. L.; Alvarez-Builla, J.
CORPORATE SOURCE:	Dep. Quim. Org., Univ. Alcala de Henares, Madrid, Spain
SOURCE:	Journal of Heterocyclic Chemistry (1986), 23(6), 1889-92 CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 107:115522

IT **96748-68-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with diketones)

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     FILE 'REGISTRY' ENTERED AT 20:03:08 ON 19 MAR 2004
L1             STRUCTURE UPLOADED
L2               0 S L1 SSS SAM
L3              18 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 20:03:59 ON 19 MAR 2004

=> s l3
L4              34 L3

=> s l4 and hypertens?
          73927 HYPERTENS?
L5                7 L4 AND HYPERTENS?

=> s l4 and (hypertens? or high(5a)blood(5a)pressure?)
          73927 HYPERTENS?
        3323204 HIGH
        1125793 BLOOD
        1120964 PRESSURE?
           6445 HIGH(5A)BLOOD(5A)PRESSURE?
L6                7 L4 AND (HYPERTENS? OR HIGH(5A)BLOOD(5A)PRESSURE?)

=> d l6 abs ibib kwic hitstr 1-7

L6   ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2004 ACS on STN
AB   A review.  Long-lived structural proteins, collagen and elastin, undergo
     continual non-enzymic crosslinking during aging and in diabetic
     individuals.  This abnormal protein crosslinking is mediated by advanced
     glycation end products (AGEs) generated by non-enzymic glycosylation of
     proteins by glucose.  The AGE-derived protein crosslinking of structural
     proteins contributes to the complications of long-term diabetes such as
     nephropathy, retinopathy, and neuropathy.  AGE-crosslinks have also been
     implicated in age-related cardiovascular diseases.  Potential treatment
     strategies for these AGE-derived complications include prevention of
     AGE-formation and breaking of the existing AGE-crosslinks.  The
     therapeutic potential of the AGE-inhibitor, pimagedine (aminoguanidine),
     has been extensively investigated in animal models and in Phase 3 clin.
     trials.  This review presents the pre-clin. and clin. studies using
     ALT-711, a highly potent AGE-crosslink breaker that has the ability to
     reverse already-formed AGE-crosslinks.  Oral administration of ALT-711 has
     resulted in a rapid improvement in the elasticity of stiffened myocardium
     in exptl. animals.  Topical administration of ALT-711 was effective in
     improving the skin hydration of aged rats.  The therapeutic potential of
     crosslink breakers for cardiovascular complications and dermatol.
     alterations associated with aging and diabetes is discussed.
ACCESSION NUMBER:         2003:804088  HCAPLUS
DOCUMENT NUMBER:          140:121913
TITLE:                    Therapeutic potential of breakers of advanced
                          glycation end product-protein crosslinks
AUTHOR(S):                Vasan, Sara; Foiles, Peter; Founds, Hank
CORPORATE SOURCE:         Alteon Inc., Ramsey, NJ, 07446, USA
SOURCE:                   Archives of Biochemistry and Biophysics (2003),
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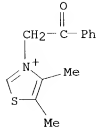
419(1), 89-96
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

IT Aging, animal
Antihypertensives
Diabetes mellitus
Human
Hypertension
(therapeutic potential of AGE crosslink breakers)

IT **341028-37-3**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; therapeutic potential of AGE crosslink breakers)

IT **341028-37-3**, ALT 711
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; therapeutic potential of AGE crosslink breakers)

RN 341028-37-3 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Renal accumulation of advanced glycation end products (AGEs) has been linked to the progression of diabetic nephropathy. Cleavage of pre-formed AGEs within the kidney by a cross-link breaker, such as ALT-711, may confer renoprotection in diabetes. STZ diabetic rats were randomized into (a) no treatment (D); (b) treatment with the AGE cross-link breaker, ALT-711, weeks 16-32 (DALT early); and (c) ALT-711, weeks 24-32 (DALT late). Treatment with ALT-711 resulted in a significant reduction in diabetes-induced serum and renal AGE peptide fluorescence, associated with decreases in renal carboxymethyllysine and RAGE immunostaining. Crosslinking of tail tendon collagen seen in diabetic groups was attenuated only by 16 wk of ALT-711 treatment. ALT-711, independent of treatment duration, retarded albumin excretion rate (AER), reduced blood pressure, and renal hypertrophy. It also reduced diabetes-induced

increases in gene expression of transforming growth factor β1 (TGF-β1), connective tissue growth factor (CTGF), and collagen IV. However, glomerulosclerotic index, tubulointerstitial area, total renal collagen, nitrotyrosine, protein expression of collagen IV, and TGF-β1 only showed improvement with early ALT treatment alone. This study demonstrates the utility of a cross-link breaker as a treatment for diabetic nephropathy and describes effects not only on renal AGEs but on putative mediators of renal injury, such as prosclerotic cytokines and oxidative stress.

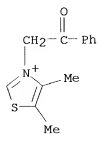
ACCESSION NUMBER: 2003:730751 HCAPLUS
DOCUMENT NUMBER: 139:301751
TITLE: The breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in experimental diabetes
AUTHOR(S): Forbes, Josephine M.; Thallas, Vicki; Thomas, Merlin C.; Founds, Hank W.; Burns, Wendy C.; Jerums, George; Cooper, Mark E.
CORPORATE SOURCE: Division of Diabetic Complications, Baker Medical Research Institute, Melbourne, 8008, Australia
SOURCE: FASEB Journal (2003), 17(12), 1762-1764, 10.1096/fj.02-1102fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **Hypertension**
(renal, reduction by cross-link breaker ALT-711; breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in exptl. diabetes)

IT **341028-37-3**, ALT 711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in exptl. diabetes)

IT **341028-37-3**, ALT 711
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; breakdown of pre-existing advanced glycation end products is associated with reduced renal fibrosis in exptl. diabetes)

RN 341028-37-3 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



● Cl⁻

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AB The invention provides a method of treating, ameliorating, or preventing certain fibrotic diseases or other indications in an animal, including a human, comprising administering an effective amount of a heterocyclic compound The effect of 3-(2-phenyl-2-oxoethyl)-4,5-dimethylthiazolium salt in a rat heart infarction model is presented.

ACCESSION NUMBER: 2002:521411 HCAPLUS
DOCUMENT NUMBER: 137:73284
TITLE: Method using heterocyclic compounds for treating fibrotic diseases or other indications
INVENTOR(S): Wagle, Dilip; Gall, Martin; Bell, Stanely C.; Lavoie, Edmond J.
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053101	A2	20020711	WO 2001-US50824	20011228
WO 2002053101	A3	20030123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1359911	A2	20031112	EP 2001-992443	20011228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002107245	A1	20020808	US 2001-38117	20011231

PRIORITY APPLN. INFO.: US 2000-259424P P 20001229
US 2001-259254P P 20010102

US 2001-296256P P 20010606
WO 2001-US50824 W 20011228

OTHER SOURCE(S): MARPAT 137:73284

IT Alzheimer's disease
Anti-Alzheimer's agents
Antiarteriosclerotics
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antihypertensives
Antitumor agents
Arteriosclerosis
Asthma
Atherosclerosis
Cardiovascular agents
Cataract
Diabetes mellitus
Dialysis
Fibrosis
Human
Hypertension
Nervous system agents
Osteoarthritis
Periodontium, disease
Rheumatoid arthritis
Sickle cell anemia
(heterocyclic compds. for treatment of fibrotic diseases or other conditions)

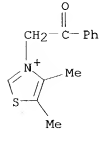
IT Blood pressure
(systolic, systolic **hypertension**; heterocyclic compds. for treatment of fibrotic diseases or other conditions)

IT **393121-34-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic compds. for treatment of fibrotic diseases or other conditions)

IT **393121-34-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic compds. for treatment of fibrotic diseases or other conditions)

RN 393121-34-1 HCAPLUS

CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Arterial stiffening with increased pulse pressure is a leading risk factor for cardiovascular disease in the elderly. We tested whether ALT-711, a novel nonenzymic breaker of advanced glycation end-product crosslinks, selectively improves arterial compliance and lowers pulse pressure in older individuals with vascular stiffening. Nine US centers recruited and randomly assigned subjects with resting arterial pulse pressures >60 mm Hg and systolic pressures >140 mm Hg to once-daily ALT-711 (210 mg; n=62) or placebo (n=31) for 56 days. Preexisting antihypertensive treatment (90% of subjects) was continued during the study. Morning upright blood pressure, stroke volume, cardiac output, systemic vascular resistance, total arterial compliance, carotid-femoral pulse wave velocity, and drug tolerability were assessed. ALT-711 netted a greater decline in pulse pressures than placebo (-5.3 vs. -0.6 mm Hg at day 56; P=0.034 for treatment effect by repeated-measures ANOVA). Systolic pressure declined in both groups, but diastolic pressure fell less with ALT-711 (P=0:056). Mean pressure declined similarly in both groups (-4 mm Hg; P<0.01 for each group, P=0.34 for treatment effect). Total arterial compliance rose 15% in ALT-711-treated subjects vs. no change with placebo (P=0.015 vs. ALT-711), an effect that did not depend on reduced mean pressure. Pulse wave velocity declined 8% with ALT-711 (P<0.05 at day 56, P=0.08 for treatment effect). Systemic arterial resistance, cardiac output, and heart rate did not significantly change in either group. ALT-711 improves total arterial compliance in aged humans with vascular stiffening, and it may provide a novel therapeutic approach for this abnormality, which occurs with aging, diabetes, and isolated systolic **hypertension.**

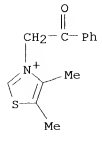
ACCESSION NUMBER: 2001:783968 HCAPLUS
DOCUMENT NUMBER: 136:112431
TITLE: Improved arterial compliance by a novel advanced glycation end-product crosslink breaker
AUTHOR(S): Kass, David A.; Shapiro, Edward P.; Kawaguchi, Miho; Capriotti, Anne R.; Scuteri, Angelo; deGroof, Robert C.; Lakatta, Edward G.
CORPORATE SOURCE: Division of Cardiology, The Johns Hopkins Medical Institutions, Baltimore, MD, 21287, USA
SOURCE: Circulation (2001), 104(13), 1464-1470
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB . . . stiffening, and it may provide a novel therapeutic approach for this abnormality, which occurs with aging, diabetes, and isolated systolic **hypertension.**

IT **181069-80-7**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; improved arterial compliance by a novel advanced glycation end-product crosslink breaker)

IT **181069-80-7**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT 711; improved arterial compliance by a novel advanced glycation end-product crosslink breaker)

RN 181069-80-7 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



● Br^-

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AB A method and compns. are disclosed for improving the elasticity or reducing wrinkles of the skin, treating disorders such as diabetes or treating or preventing adverse sequelae of diabetes, kidney damage, damage to blood vasculature, **hypertension**, retinopathy, damage to lens proteins, cataracts, peripheral neuropathy, or osteoarthritis. Thus, 3-(2-phenyl-2-hydroxyethyl)-4,5-dimethylthiazolium chloride (I)was prepared by the reduction of 2-chloroacetophenone followed by the reaction of the resulting alc. with 4,5-dimethylthiazole. Tablets contained I 50, starch 50, mannitol 75, mg stearate 2, and stearic acid 2 mg/tablet.

ACCESSION NUMBER: 2001:635892 HCAPLUS
DOCUMENT NUMBER: 135:200476
TITLE: Thiazolium compounds and treatments of disorders associated with skin aging
INVENTOR(S): Wagle, Dilip; Vasan, Sarah; Egan, Jack
PATENT ASSIGNEE(S): Alteon, Inc., USA
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062250	A1	20010830	WO 2001-US5868	20010223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002055527	A1	20020509	US 2001-792422	20010223
US 6458819	B2	20021001		
EP 1257272	A1	20021120	EP 2001-916200	20010223

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

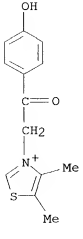
JP 2003523388 T2 20030805 JP 2001-561316 20010223
PRIORITY APPLN. INFO.: US 2000-184266P P 20000223
WO 2001-US5868 W 20010223
OTHER SOURCE(S): MARPAT 135:200476

AB . . . skin, treating disorders such as diabetes or treating or preventing adverse sequelae of diabetes, kidney damage, damage to blood vasculature, **hypertension**, retinopathy, damage to lens proteins, cataracts, peripheral neuropathy, or osteoarthritis. Thus, 3-(2-phenyl-2-hydroxyethyl)-4,5-dimethylthiazolium chloride (I)was prepared by the reduction of 2-chloroacetophenone. . . .

IT 356759-42-7P 356759-43-8P 356759-44-9P **356759-45-0P**
356759-46-1P 356759-47-2P 356759-48-3P
356759-50-7P 356759-52-9P 356759-53-0P
356759-54-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiazolium compds. for treatments of disorders associated with skin aging)

IT **356759-45-0P 356759-46-1P 356759-47-2P**
356759-50-7P 356759-52-9P 356759-53-0P
356759-54-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiazolium compds. for treatments of disorders associated with skin aging)

RN 356759-45-0 HCAPLUS
CN Thiazolium, 3-[2-(4-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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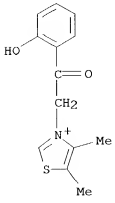
RN 356759-46-1 HCAPLUS

CN Thiazolium, 3-[2-(2-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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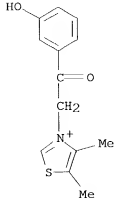
RN 356759-47-2 HCAPLUS
CN Thiazolium, 3-[2-(3-hydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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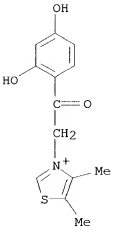
RN 356759-50-7 HCAPLUS
CN Thiazolium, 3-[2-(2,4-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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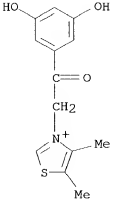
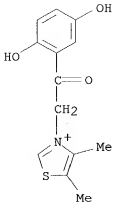
RN 356759-52-9 HCAPLUS
CN Thiazolium, 3-[2-(3,5-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



● Br^-

RN 356759-53-0 HCAPLUS
CN Thiazolium, 3-[2-(2,5-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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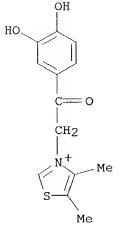
RN 356759-54-1 HCAPLUS
CN Thiazolium, 3-[2-(3,4-dihydroxyphenyl)-2-oxoethyl]-4,5-dimethyl-, bromide (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AB A review with 6 refs. Vascular and/or myocardial stiffness is a major problem in ageing, diabetes, **hypertension** and heart failure. The development of the stiffness is partly due to the formation of glucose-dependent cross-links in the collagen. ALT-711 cleaves these cross-links. In aged-rhesus monkeys, ALT-711 decreases vascular stiffness and this effect is reversible. ALT-711 also decreases myocardial

stiffness in the monkeys but this effect is not reversible in 39 wk. ALT-711 has potential in the treatment of the stiffness associated with diabetes, **hypertension** and heart failure.

ACCESSION NUMBER: 2001:321927 HCAPLUS
DOCUMENT NUMBER: 135:131603
TITLE: ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure
AUTHOR(S): Doggrell, Sheila A.
CORPORATE SOURCE: Doggrell Biomedical Communications, Auckland, N. Z.
SOURCE: Expert Opinion on Investigational Drugs (2001), 10(5), 981-983
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

TI ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure

AB A review with 6 refs. Vascular and/or myocardial stiffness is a major problem in ageing, diabetes, **hypertension** and heart failure. The development of the stiffness is partly due to the formation of glucose-dependent cross-links in the collagen.. . . this effect is not reversible in 39 wk. ALT-711 has potential in the treatment of the stiffness associated with diabetes, **hypertension** and heart failure.

ST review cardiovascular stiffness ALT711 diabetes **hypertension**; heart failure arterial stiffness ALT711 review

IT Aging, animal
Diabetes mellitus
Hypertension
(ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

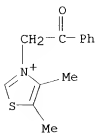
IT Heart, disease
(failure; ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

IT Artery, disease
(stiffness; ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

IT **341028-37-3**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

IT **341028-37-3**, ALT 711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ALT-711 decreases cardiovascular stiffness and has potential in diabetes, **hypertension** and heart failure)

RN 341028-37-3 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, chloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AB Nonenzymic glycosylation and crosslinking of proteins by glucose contributes to an age-associated increase in vascular and myocardial stiffness. Some recently synthesized thiazolium compds. selectively break these protein cross-links, reducing collagen stiffness. We investigated the effects of 3-phenacyl-4,5-dimethylthiazolium chloride (ALT-711) on arterial and left ventricular (LV) properties and their coupling in old, healthy, nondiabetic Macaca mulatta primates (age 21±3.6 yr). Serial measurements of arterial stiffness indexes [i.e., aortic pulse wave velocity (PWV) and augmentation (AGI) of carotid arterial pressure waveform] as well as echocardiog. detns. of LV structure and function were made before and for 39 wk after 11 i.m. injections of ALT-711 at 1.0 mg/kg body weight every other day. Heart rate, brachial blood pressure, and body weight were unchanged by the drug. PWV and AGI decreased to a nadir at 6 wk [PWV to 74.2±4.4% of baseline (B), P = 0.007; AGI to 41±7.3% of B, P = 0.046], and thereafter gradually returned to baseline. Concomitant increases in LV end diastolic diameter to 116.7±2.7% of B, P = 0.02; stroke volume index (SVindex) to 173.1±40.1% of B, P = 0.01; and systolic fractional shortening to 180±29.7% of B, P = 0.01 occurred after drug treatment The LV end systolic pressure/SVindex, an estimate of total LV vascular load, decreased to 60±12.1% of B (P = 0.02). The LV end systolic diameter/SVindex, an estimate of arterio-ventricular coupling, was improved (decreased to 54.3±11% of B, P < 0.002). Thus, in healthy older primates without diabetes, ALT-711 improved both arterial and ventricular function and optimized ventriculo-vascular coupling. This previously unidentified cross-link breaker may be an effective pharmacol. therapy to improve impaired cardiovascular function that occurs in the context of heart failure associated with aging, diabetes, or **hypertension**, conditions in which arterial and ventricular stiffness are increased.

ACCESSION NUMBER: 2001:120548 HCAPLUS

DOCUMENT NUMBER: 134:290192

TITLE: A cross-link breaker has sustained effects on arterial and ventricular properties in older rhesus monkeys

AUTHOR(S): Vaitkevicius, Peter V.; Lane, Mark; Spurgeon, Harold; Ingram, Donald K.; Roth, George S.; Egan, John J.; Vasan, Sara; Wagle, Dilip R.; Ulrich, Peter; Brines, Michael; Wuerth, Jean Paul; Cerami, Anthony; Lakatta, Edward G.

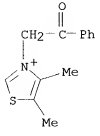
CORPORATE SOURCE: Intramural Research Program, Gerontology Research Center, National Institute on Aging, National Institutes of Health, Baltimore, MD, 21224, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(3), 1171-1175
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB . . . pharmacol. therapy to improve impaired cardiovascular function that occurs in the context of heart failure associated with aging, diabetes, or **hypertension**, conditions in which arterial and ventricular stiffness are increased.

IT **181069-80-7**, ALT-711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of cross-link breaker on arterial and ventricular properties in aging rhesus monkeys)

IT **181069-80-7**, ALT-711
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of cross-link breaker on arterial and ventricular properties in aging rhesus monkeys)

RN 181069-80-7 HCAPLUS
CN Thiazolium, 4,5-dimethyl-3-(2-oxo-2-phenylethyl)-, bromide (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT